REMARKS

Claims 1 to 26 are in the application. Claims 13 to 26 have been added. Claims 6 and 12 have been amended to correct a typographical error. Claim 6 has now been broken into an additional four species claims as claims 6, and 15 to 19, with composition of matter claims added for each of the species claims. Support for added claims 13 and 14 lies in the specification on page23, lines 3 to 42 and page 4, lines 1 to 10. No new matter is believed added.

The Examiner comments that the Information Disclosure Statement filed 31 January 2005 fails to comply with 37 CFR 1.98(a)(2) which is stated to "requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed".

The present application is the §371 national stage entry of PCT/GB2003/00316. Applicants do not need to send in the foreign patents, or other cited reference from the International PCT search report as they have previously been forwarded to the USPTO from WIPO. Applicants merely submit the 1449 form for the Examiner's convenience to note that they have been considered. Should the Examiner not have such references in the file, please advise Applicants attorney at the number indicated below and they will be resubmitted accordingly. Consequently, Applicants again request that the Examiner review the list of citations cited on the 1449 form submitted on 31 January 2005. A clean copy of said form is attached with this response.

Rejection under 35 USC §103

Claims 1 to 3, 5 and 7 to 11 are rejected under 35 USC§103(a) as being unpatentable over WO 2003/097610, Martina et al. Applicants respectfully traverse this rejection.

The Examiner comments that "[T]he '610 publication discloses several compounds which would anticipate Applicant's Markush language of Claim 1, with the exception that Applicant's instant genus must contain a methyl or chloro at the R1 position." See Page 5, lines 6 to 8 (Office Action).

The '610 publication is simply that, a WO publication effective as of 27 November 2003. The publication is not effective as of its filing date unless it has entered

the US and published therein. Applicants are unable to find a corresponding US publication. Applicant's priority application was filed 31 July 2002. The PCT application was filed 30 July 2003. Consequently, the Martina et al. WO publication is an application which has a later date, e.g. that of 27 November 2003, and is not an effective publication against the claims of the present application under the provisions of 35 USC §103(a).

In view of this, withdrawal of the rejection to the claims under 35 USC 103 is respectfully requested.

Rejection under 35 USC §103

Claims 1 to 5, 7 and 11 are rejected under 35 USC §103(a) as being unpatentable over US 2004/0110802A1 ('802), Thoarensen et al. Applicants respectfully traverse this rejection.

The Examiner comments that the "same rationale as that of the improper rejection under WO 2003/097610 publication applies, e.g. that the '802 publication discloses compound which would anticipate Applicant's claimed genus, with the exception that Applicant's instant genus must contain a methyl or chloro at the R1 position. The compounds disclosed in the '802 publication disclose hydrogen at the equivalent position. Alternatively Applicant's claimed genus encompasses compounds which simply add a methyl to known compounds." (See Page 7, Point 2, Office Action).

Applicants have fulfilled all the requirements under the provisions of 35 USC §119 for a claim to priority to that of their 31 July 2002, as so noted by the Examiner on the accompanying PTOL 326 form. Consequently, this should remove the rejection made by the Examiner under 35 USC §103 herein. In fact, Applicants should be cited as prior art against the application of Thorarensen.

In view of these remarks, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

Obvious Double Patenting Rejection

Claims 1 to 5 and 7 to 11 are provisionally rejected under the judicially crated doctrine of obviousness-type double patenting as being unpatentable over Claims 1 to 13, 15, 16, and 18-2 of Applicants co-pending application USSN 10/587,790. Applicants respectfully traverse this rejection.

Applicants copending application 10/587,790 corresponds to that of WO 2005/073217. The 10/587,790 application is the junior application. The 10/587,790

application has a priority date of 30 January 2004. As noted above, the present application has a priority date of 31 July 2002.

The MPEP 804 section quoted by the examiner on page 10 of the Office Action is quite clear as to the process which should occur. In this instance the earlier-filed application (the instant one) should be permitted to issue as a patent without a terminal disclaimer. The later-filed application will be handled accordingly upon examination.

Rejection under 35 USC §112

Claims 8 and 9 are rejected under 35 USC §112, first paragraph as being non enabling for treating "any condition or disease state mediated by p38 kinase activity in a patient" or "for treating any condition or disease stated mediated by cytokines produced by the activity of p38 kinase in a patient." Applicants respectfully traverse this rejection.

The Examiner states that Applicants do provide working examples in the specification and that these examples demonstrate certain of the claimed compounds' ability to inhibit p38 kinase in vitro. "There is no evidence correlating the *in vitro* date to *in vivo* usage as claimed in Claims 8 and 9." (Office Action, page 4, 2nd paragraph).

With respect to the state of the art at the time the application was filed, the signaling pathway of p38 kinase had been extensively studied. Applicants have previously submitted a review article on signaling cascades in inflammatory diseases (see Herlaar, E. et al., Molecular Med Today (1999), Vol. 5, 439-447). This article and several additional articles on p38 kinase inhibitors also previously submitted detail the linkage of the p38 cascade to a number of acute and chronic inflammatory diseases, such as RA, osteoarthritis, inflammatory bowel disease, toxic shock syndrome, septic shock, asthma, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), and osteoporosis. The skilled artisan would also have available many more later articles describing the role of the pro-inflammatory cytokine in the diseases enumerated herein.

Consequently, use of p38 inhibitors for the treatment of inflammatory diseases, such as rheumatoid arthritis, psoriasis, COPD, and asthma, etc. is known in the art. In view of this Applicants have added a claim directed to these particular disease states, dependent upon claim 8.

The specification further provides sufficient information on how to make and how to use the compound as claimed herein. See for example pages 18, lines 15 to 43 through page 22, lines 1 to 39 which describe how to formulate, how to dose, and how to administer the compounds of Formula (I). Therefore, Applicants believe that

the specification is sufficiently enabled and would not require undue experimentation to practice the invention.

There is no requirement that actual in vivo data be presented in an application in order to meet the written description requirement. The p38 Kinase Assay is a very well known, and art recognized method in the art, having been taught in a number of applications and US patents for quite a number of years.

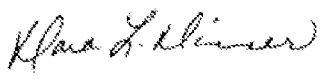
The Examiner has not demonstrated a reasonable basis, other than speculation, that the compounds herein would not possess their p38 inhibitory activity in vivo. In fact, there are large numbers of papers prior to the time of filing of this application wherein p38 inhibitors have been taken into in vivo models and demonstrated inhibitory activity. Should the Examiner require submission of some of these papers or preclinical models please advise the undersigned.

In view of these remarks, reconsideration and withdrawal of the rejection under 35 USC §112 to claims 8 and 9 is respectfully requested.

Claims 6 and 12 were noted as being allowable but for the dependence on a rejected base claim. As it is believed that any rejections to the base claims have been overcome, all the claims in the application are believed to be in condition for allowance.

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any additional fees or charges are required by this paper the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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